Accepted Manuscript

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PII: S1389-9457(15)00087-8
DOI: http://dx.doi.org/doi:10.1016/j.sleep.2014.12.015
Reference: SLEEP 2671

To appear in: *Sleep Medicine*

Received date: 2-9-2014
Revised date: 15-12-2014
Accepted date: 15-12-2014

Please cite this article as: Ottavio Vitelli, Alessandra Tabarrini, Silvia Miano, Jole Rabasco, Nicoletta Pietropaoli, Martina Forlani, Pasquale Parisi, Maria Pia Villa, Impact of obesity on cognitive outcome in children with sleep disordered breathing., *Sleep Medicine* (2015), http://dx.doi.org/doi:10.1016/j.sleep.2014.12.015.

Title: Impact of obesity on cognitive outcome in children with sleep disordered breathing.

Subtitle: Obesity and cognitive outcome in children with sleep disordered breathing

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Financial Disclosure: This study did not receive financial support

Conflict of interest: None of the authors have potential conflicts of interest to be disclosed

Highlights:

- Obese children with OSA had lower T-IQ and P-IQ scores than other groups.
- Obese children with OSA had higher performance impairment at the subtest.
- RDI and BMI percentile predicted the negative outcome of T-IQ in obese OSA children.

Abstract

Objectives: To evaluate the impact of obesity on cognitive impairment, in children with obstructive sleep apnea (OSA), children with OSA and obesity and in normal controls.

Methods: Thirty-six children with OSA (group1), 38 children with OSA and obesity (group2) and 58 normal controls (group3) were studied. Total-intelligence quotient (T-IQ), verbal-IQ (V-IQ) and the performance-IQ (P-IQ) scores, were obtained using the Wechsler Intelligence Scale for Children–Third Edition Revised. All participants' parents filled out attention deficit and hyperactive disorder rating scale to investigate symptoms of hyperactivity and attention deficit. Obese and non-obese children with sleep disordered breathing (SDB) performed polysomnography.

Results: T-QI and P-QI scores were significantly lower in group 2 with higher performance impairment at the subtest compared to other groups. In obese children, V-IQ was significantly correlated with age of onset (r=0,335,p=0,05) and duration of SDB (r=-0,362,p=0,02),while, P-IQ and T-IQ were correlated with BMI percentile (r=-0,341,p=0,03) and RDI (r=-0,321,p=0,05) respectively. RDI and BMI negatively influenced T-IQ in obese children with OSA. No correlation was found between sleep parameters and IQ scores or subtest scores in all groups.

Conclusions: Obese children with OSA showed higher cognitive impairment. Obesity has an additive and synergic action with that exerted by OSA, speeding-up complications' onset.

Keywords: Obesity, sleep disordered breathing, children, cognitive impairment

1.Introduction

Sleep disordered breathing (SDB) is a common condition in children that includes the broad spectrum of pathology ranging from primary snoring to obstructive sleep apnea syndrome (OSA). OSA in children is a "disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns" [1]. Symptoms include habitual snoring, apnoea, restless sleep, and diurnal neurobehavioural problems, such as attention deficit and hyperactive disorder (ADHD), learning problems, behavioural disorders and hypersomnolence [2-4]. Findings from previous research suggest that intermittent hypoxia during sleep and sleep fragmentation are the main causative factors involved in the pathogenesis of neurocognitive impairment of SDB [3-9].

Recently, the results of the Childhood Adenotonsillectomy Trial (CHAT) have been published and have clearly confirmed that neurocognitive and behavioural dysfunctions in children with OSA are consistent and partially reversible [10]. CHAT was a multicenter, single-blind, randomized, controlled trial in seven academic paediatric sleep centers in the USA designed to evaluate the efficacy of early adenotonsillectomy in comparison with watchful waiting with supportive care, with respect to cognitive, behavioural, quality-of-life, and sleep factors in children with OSA, including obese children, during 7 months of follow-up, As compared with a strategy of watchful waiting, surgical treatment for the obstructive sleep apnoea syndrome in school-age children did not significantly improve attention or executive function as measured by neuropsychological testing but did reduce symptoms and improve secondary outcomes of behaviour, quality of life, and polysomnographic findings.

Most studies have failed to find a direct correlation between SDB severity and cognitive and behavioural problems [11,12]. It seems to be no direct dose–response relationship between disease severity and cognitive outcomes. This has led to hypothesis that other factors, such as genetic susceptibility, environmental influences, co-morbid conditions, such as obesity, shortened sleep duration, and the presence of other sleep disorders, may also influence neurocognitive outcomes. A prospective non-randomized study of children undergoing a diagnostic assessment for SDB, compared to normal controls, demonstrated that ADHD rating scale scores was higher in children with SDB, and intelligence quotient (IQ) estimate lower, with significant correlations with sleep microstructure, analyzed by cyclic alternating pattern (CAP) and cardio-respiratory parameters [13]. These data confirmed that other factors during sleep may influence cognitive outcome in OSA children.

Obesity is considered one of the most important risk factor for OSA [14,15] and preliminary evidences suggest that it is an independent contributor to cognitive functioning [16]. One study demonstrated that Performance-IQ (P-IQ) score was markedly lower in overweight/obese patients than those with normal weight, with a significant positive correlation between the P-IQ score and body mass index (BMI) [17]. OSA in the context of obesity may independently or synergistically affect neurocognitive function and maturation.

The aim of this study was to evaluate the effect of obesity on neurocognitive disability of children with OSA, measuring IQ, and ADHD symptoms in children with OSA, in children with OSA and obesity and in normal controls.

2.Methods

2.1 Subjects

Children with SDB undergoing their first diagnostic assessment for OSA in our Paediatric Sleep Centre (Rome, Italy) were consecutively enrolled between January 2013 and December 2013. Patients with a history of any systemic diseases or major neurological or psychiatric disorders (such as autism, epilepsy and headache), previous treatment for OSA (including tonsillectomy and adenoidectomy, or orthodontic treatment), acute or chronic cardiorespiratory or neuromuscular diseases, dysmorphism, major craniofacial abnormalities were excluded. Patients with familial history of major neurological or psychiatric disorders, any type of mental retardation or known genetic syndromes were also excluded.

A detailed personal and family history was obtained for all the participants and a clinical examination was performed. Moreover parents were asked when their child started to present night-time symptoms (like snoring apnea and restless sleep). Disease duration was defined as the time between onset of symptoms and our evaluation.

Body weight was determined to the nearest 0.05 Kg, and height was measured to the nearest 0.1 cm using standardized measuring equipment. The measurements were taken in the morning after urination, wearing only underwear. BMI was calculated in kilograms per square meter and then converted to a sex- and age-specific BMI percentile value. Children were categorized using standard BMI-growth curves for age and gender criteria according to International Obesity Task Force (IOFT) cut-off points. Children underwent a laboratory polysomnography (PSG) in our sleep centre after one night of adaptation.

Control children age- and sex-matched were also recruited from two schools in the same urban area of the study groups. They were of Caucasian origin and of middle socioeconomic status. Inclusion criteria were: normal healthy prepubertal children had normal sleep habits; none of the controls was obese or had any serious physical, neurological or psychiatric disorder. No history of sleep problems (snoring, apneas, restless sleep) were reported, as demonstrated by negative Brouillette score [18], and none was taking medication at the time of testing. Control group underwent only cognitive assessment.

Moreover, we analysed the parental educational score. This score was calculated by summing mother and father instruction scores, using the following parameters: did not complete primary school = 1; completed primary school = 2; completed middle school = 3; dropped out of high school = 4; completed high school = 5; dropped out of university = 6; completed university = 7.

The local ethics committee approved the study protocol and all children's parents gave their informed consent to the procedures.

2.2 Cognitive assessment

IQ was obtained using the Wechsler Intelligence Scale for Children – Third Edition Revised (WISC-R, 1973; Rubini and Padovani, 1986), an intelligence test validated for children between the age of 6 and 16 years whose administration usually requires 75-80 minutes.

The test comprises 10 core subtests and two supplemental tests. These subtests generate a full scale score, total-IQ (T-IQ), and two composite scores known as indexes: the Verbal-IQ (V-IQ), (including Vocabulary, Similarities, Comprehension, Information, Arithmetic, and Digit Span as supplemental test) and the P-IQ, (including Block Design, Picture Stories, Picture Completion, Puzzle, Coding and Mazes as supplemental test). The IQ testing was performed in the morning before the sleep study. A Wechsler score <70 was considered to indicate mental retardation, while a Wechsler score <85 was considered to indicate borderline intellectual functioning, according to the Statistical Manual of Mental Disorders, Fourth Edition axis II diagnosis (1994).

All participants' parents filled out the ADHD-Rating Scale [19], a clinical interview that recognizes symptoms of hyperactivity and inattention according to the Diagnostic and Statistical Manual of Mental Health Disorders, Fourth Edition. It consists of 18 items, divided into two subgroups of 9 questions that investigate inattention and hyperactivity symptoms. Our purpose was investigating symptoms of hyperactivity and presence of attention deficit rather than diagnose ADHD syndrome.

2.3 Polysomnographic parameters

All patients underwent a full-night PSG in our Sleep Centre after one night of adaptation. Standard overnight PSG recordings were obtained using a Grass Heritage polygraph. The variables recorded included: a 6- channel electroencephalogram (bilateral frontal, central temporal and occipital monopolar montages referred to the contralateral mastoid); an electrooculogram (electrodes placed 1 cm above the right outer cantus and 1 cm below the left outer cantus and referred to A1); a submental electromyogram and electrocardiogram (1 derivation). Sleep was subdivided into 30-s epochs, and sleep stages were scored according to the standard criteria of the AASM [20]. The following conventional sleep parameters were measured: total sleep time, defined as the time from sleep onset to the end of the final sleep stage; sleep efficiency, defined as the percentage ratio between total sleep time and total recording time (from lights-out clock time to lights-on clock time); wakefulness after sleep onset, defined as the time spent awake between sleep onset and the end of sleep. The percentage of total sleep time in each stage was measured as follows: percentage of stage N1, stage N2, stage N3, and REM sleep.

Respiratory events were counted according to the criteria established by the AASM [21].

Obstructive apnoea was scored when there was a ≥ 90% drop in the signal amplitude of airflow for at least the duration of 2 breaths during baseline breathing, associated with the presence of respiratory effort throughout the entire period of absent airflow. Central apnoea was defined as the absence of airflow, with the cessation of respiratory effort, lasting more than 20 seconds or lasting at least two missed breaths (or the duration of two baseline breaths), associated with an arousal, an awakening or a ≥3% desaturation; central apnoea occurring after gross body movements or after sighs was not considered as a pathological finding. Mixed apnoea was defined as apnoea that usually began as central and ended in obstruction, according to changes in the chest, abdominal and flow traces. An event was scored as hypopnea if there was a peak signal excursions drop by ≥ 30% of pre-events baseline lasting for at least 2 breaths, associated to ≥ 3% desaturation from pre-event baseline or with an arousal. A respiratory events were scored as a respiratory effort-related arousals (RERA) if there was a sequence of breaths lasting at least 2 breaths when the breathing sequence was characterized by increasing respiratory effort, flattening of the inspiratory portion of the nasal pressure and snoring, leading to arousal from sleep.

Chest and abdominal movements were measured by strain gauges. Oronasal airflow was monitored in all the children with a thermocouple and nasal pressure evaluation was added if nasal cannula was tolerated. Arterial oxygen saturation was monitored with a pulse oximeter. The respiratory disturbance index (RDI) was defined as the average number of apnoeas, hypopnoeas and RERA per hour of sleep.

All recordings started at patients' usual bedtime and continued until spontaneous awakening.

The diagnosis of OSA was confirmed by laboratory polysomnography (PSG) revealing an obstructive RDI > 1, according to the criteria of the American Academy of Sleep Medicine [20]. Primary snoring was diagnosed in children with habitual snoring, an RDI <1, and microphone-detected snoring.

2.4 Study design

According to the BMI we defined 2 study groups: subjects with SDB without obesity (BMI percentile ≤ 95th) (Group 1) and children with SDB and obesity (BMI percentile >95th) (Group 2). We compared study groups with age- and sex-matched school-age healthy children (Group 3)

2.5 Statistical analysis

Data are expressed as mean ± SD. The Mann-Whitney test and Student's t test, Spearman and Pearson tests, χ^2 test were chosen, when appropriate. Differences and correlations were considered as statistically significant when $p < 0.05$.The statistical analysis was performed using a commercial software package (SPSS, version 11; SPSS; Chicago, IL).

3. Results

We studied 36 children with OSA (group 1: M/F 21/15, mean age 8,29 ± 2,04, mean BMI percentile 62,61 ± 29,65), 38 children with OSA and obesity (group 2: M/F 27/11, mean age 8,73 ± 2,04, mean BMI percentile 116,52 ± 15,95) and 58 normal controls (group 3: M/F 29/29; mean age 8,89 ± 1,62 years). No differences in age and sex were found in the three groups (table 1). No differences emerged in parental educational score between the three groups (group 1: mean 10,6 ± 2, group 2: mean 10,5 ±2,4; group 3: mean 11,3 ±2). In group 1, age of onset of SDB was significantly lower and disease duration was significantly longer compared to group 2. No significant differences emerged in sleep macrostructure, arousal index and respiratory parameters if we exclude that obese children had a lower minimal overnight oxygen saturation and a higher REM percentage than children with only OSA.

Control group showed higher IQ scores in comparison with groups 1 and 2 while T-QI and P-QI scores were significantly lower in group 2 than in other groups and V-IQ was greater among children with OSA compared to non-OSA (table 2). Group 1 and 2 had 5/5 verbal subtest significantly lower compared to

controls, while 2/5 (group 1) and 4/5(group 2) performance subtest were significantly lower compared to controls (Table 2).

Only in non obese OSA children, P-IQ was significantly correlated with age of onset of respiratory symptoms (r= 0,335, p<0,05). On the other hand, in obese children, V-IQ was significantly correlated with age of onset (r= 0,335, p<0,05) and duration of SDB (r= -0,362, p<0,05), while, P-IQ and T-IQ were correlated with BMI percentile (r= -0,341, p=0,03) and RDI (r= -0,321, p<0,05) respectively (Table 3). No correlation was found between sleep stages, arousal index, oxygen saturation and IQ scores or subtest scores in all groups.

According to ADHD rating scale scores we identified hyperactivity symptoms in 13/36 (36,1%) and in 7/38 (18,%) patients in group 1 and group 2 respectively, while inattention symptoms were present in 12/36 (33%) and in 9/38 (23,7%). None of control children showed hyperactivity or inattention symptoms (Table 4).

In patient with obesity and OSA, stepwise multiple linear regression, identified RDI and BMI percentile as the variables that negatively influenced T-IQ (table 5), using as independent values T-IQ and as dependent values RDI, duration of SDB and age of onset of symptoms, BMI and BMI percentile.

4. Discussion

Our study evaluated the impact of obesity on IQ in children with OSA and demonstrated that obesity is an important risk factor for developing cognitive impairment.

Childhood obesity has reached epidemic proportions worldwide, with prevalence rates ranging from 7% to 22% of children [22,23]. It is now recognized as a major health problem that is already associated with several physical, psychosocial, and social consequences [24].

Studies examining the prevalence of OSA in children have shown substantial increases with obesity such that the risk of OSA increases by 12% for each increase of 1 kg/m2 of BMI above the mean in children, resulting in a prevalence ranged between 13% and 59% in obese children, compared to 2–3% in normal-weight children [13,15,25,26]. Structural changes in the upper airway, adenotonsillar hypertrophy, and excess fat deposition around the pharynx may be responsible for the increased risk of OSA in obese children [27,28].

Several studies have shown that children aged 3–5 undergo significant and rapid development of executive and cognitive functions which continues to mature into adolescence [29,31]. Each region of prefrontal cortex, which is associated with executive and cognitive functions, may have its own developmental trajectory and timeline [30,31]. Therefore, each function is quite vulnerable to a stressor such as OSA and

obesity during childhood. Obesity and OSA have a detrimental effect on the brain since both can lead to cognitive impairment [32].

Our data revealed a lower T-IQ and P-IQ in patient with OSA and obesity compared with non-obese children and controls. Moreover, BMI was negatively correlated with P-IQ scores in obese patients with OSA. All children with OSA showed 5/5 verbal subtests impaired compared with controls. Obesity seems to be a cumulative risk factor for performance impairment since group 2 showed lower scores on 4/5 P-IQ subtests compared with controls while children with only OSA presented just 2/5 subtests impaired. It has been previously demonstrated that patients with OSA showed lower verbal retention compared to healthy subjects [33]. Our results showed lower V-QI in children with OSA compared to non-OSA.

The way in which obesity may influence cognitive function and in particular P-IQ can be explained looking at the correlations between some limbic areas and obesity and cognitive process. Amygdala, prefrontal cortex and nucleus accumbens (which is considered the neural interface between motivations and actions) dynamically interact in order to control goal-directed behaviour throughout dopamine release regulation [17,34,35]. Dopamine system is itself involved in feeding, reward and goal-directed behaviour. So these limbic structures might represent the networks that are responsible for the lower score achieved at the P-IQ by obese children [17,34,35].

In addition to this, we have to consider that OSA is characterized by intermittent hypoxia that induced neuronal injury especially in prefrontal regions of the brain cortex, as it has been previously hypothesized by Beebe and Gozal [3].

It is important to underline that a longer exposure to the effects of SDB, especially while prefrontal cortex is developing, may lead to cognitive impairment. In our groups, a precocious age of onset of sleep respiratory problems in preschool-age and a longer duration of disease resulted in lower P-IQ and V-IQ scores. Even though obese children showed a significantly higher age of onset and lower duration of OSA compared to non-obese patients, they showed a greater cognitive impairment. It is not unreasonable to assume that obesity in these patients has an additive and synergic action in addition to that exerted by OSA, speeding up the onset of complications. In this patients, logistic linear regression, demonstrated that T-QI is influenced by the combination of severity of disease and BMI percentile.

We did not find any correlations with sleep parameter such as sleep stages and arousal index. These findings are apparently in disagreement with previous reporting that sleep fragmentation might lead to cognitive impairment [36,37] These studies have evaluated sleep disruption through finer methods that allow to identify microarousals and periodic EEG activity in NREM sleep which is related to fluctuations in the level of arousal that characterize two different functional states in the arousal control mechanism [36-

38]. Thanks to these methods it is possible to evaluate the presence of microarousals and EEG disruption able to produce significant impact on cortical activity and neurobehavioral outcomes.

There is a well-established correlation between sleep disturbances and ADHD symptoms [4] and several studies have investigated the relationship between observed IQ scores and attention deficits in children and adolescents with diagnosis of ADHD [39,40] demonstrating that it is generally modest, with the mean influence on IQ probably amounting to 2 to 5 IQ points .

We have to consider that ADHD has several phenotypes and some authors have suggested that ADHD represents one extreme of the quantitative manifestation of normal behavior [41,42]. Since there are no questionnaires that are able to capture these nuances, we have administered the ADHD-Rating Scale with the purpose to investigate symptoms of hyperactivity and presence of attention deficit and not to diagnose ADHD syndrome. In our children, low IQ scores should be the result of attention deficits during WISC test administration.

The study demonstrated the effect of obesity on neurocognitive disability of children with OSA and obesity, measuring IQ. However our results should be viewed in the context of one important limitation. The absence of a group of obese patients without OSA did not allow us to investigate the influence of obesity alone and how it independently impairs cognitive function, by comparing the effect of obesity on control subjects. However, it has been demonstrated that an increasing BMI was associated with lower cognitive function, suggesting a linear relationship and previous findings showed significantly lower cognitive indices in obese individuals compared with those with normal weight [43-45]. Moreover it has to be considered that the age of onset of symptoms was parental reported and this could have influenced also the assessment of disease duration.

5. Conclusions

In conclusion, we demonstrate that obesity in OSA children had a negative influence on IQ. Performance-IQ was impaired in all patients presenting with SDB even if obese children showed lower scores at the P-IQ subtests in comparison with controls.

Moreover, since age of onset, duration and severity of OSA and BMI percentile seem to play an important role in the development of cognitive impairment, clinicians should be alerted that the recognition and treatment of both OSA and obesity is of vital importance and urgency in children.

Given the clinical importance of cognitive complaints there is a clear need for future studies on the interaction between OSA and obesity.

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Table 1. Anthropometric, clinical and polysomnographic characteristics, in children with obstructive sleep apnea syndrome without obesity (Group 1), children with obstructive sleep apnea syndrome and obesity (Group 2), and controls children (Group 3). All diffefferences are considered statistically significant if p<0,05.

	Non obese children with obstructive sleep apnea syndrome (Group 1) N=36	Children with obstructive sleep apnea syndrome and obesity (Group 2) N=38	Control group (Group 3) N=58	Kruskal Wallis Test p	Mann-Whitney Test p		
					1 vs 2	2vs3	1vs3
Age (years)	8,29 ± 2,04	8,73 ± 1,69	8,89 ± 1,62	NS			
BMI (kg/m^2)	17,76 ± 2,78	26,05 ± 3,48	17,31 ± 1,92	0,001	0,001	0,001	NS
BMI Percentile	62,61 ± 29,65	116,52 ± 15,95	59,89 ± 22,25	0,001	0,001	0,001	NS
Duration of disease (months)	47,75 ± 27,72	34,21 ± 27,22	-	-	0,03	-	-
Age of onset of disease (years)	4,34 ± 2,79	6,22 ± 3,06	-	-	0,01	-	-
RDI (ev/h)	6,27 ± 8,17	4,98 ± 4,51	-	-	NS	-	-
Overnight oxygen saturation (%)	97,16 ± 1,31	97,20 ± 0,98	-	-	NS	-	-
Minimal overnight oxygen saturation	93,21 ± 3,68	91,74 ± 3,57	-	-	0,05	-	-
N1 (%)	8,49 ± 4,47	9,05 ± 6,45	-	-	NS	-	-
N2 (%)	36,15 ± 9,28	37,67 ± 8,40	-	-	NS	-	-
N3 (%)	33,35 ± 10,28	31,36 ± 7,77	-	-	NS	-	-
REM (%)	16,96 ± 7,20	19,91 ± 5,95	-	-	0,04	-	-

Total sleep time (min)	418,11 ± 81,79	400,31 ± 71,24	-	-	NS	-	-
Wakefulness after sleep onset (min)	43,39 ± 42,43	56,59 ± 48,61	-	-	NS	-	-
Sleep efficiency (%)	85,58 ± 11,01	83,57 ± 14,01	-	-	NS	-	-

Respiratory disturbance index, RDI ; Body mass index BMI

Table 2. Comparison between WISC-R scale intellicence quotient estimates, verbal intelligence quotient subtests (Vocabulary, Similarities, Comprehension, Information, Arithmetic) and performance intelligence quotient subtests (Block Design, Picture Stories, Picture Completion, Puzzle, Coding) in children with sleep-disordered breathing (Group 1), children with sleep-disordered breathing and obesity (Group 2), and controls children (Group 3). All diffefferences are considered statistically significant if p<0,05

	Children with sleep disordered breathing (Group 1) N=36	Children with sleep disordered breathing and obesity (Group 2) N=38	Control group (Group 3) N=58	Mann-Whitney Test p		
				1 vs 2	2vs3	1vs3
T-QI	98,11 ± 12,68	91,78 ± 16,11	109,63 ± 12,04	0,02	0,001	0,001
P-QI	100,63 ± 14,98	93,92 ± 14,89	117,27 ± 11,96	0,03	0,001	0,001
V-QI	96,75 ± 13,51	91,81 ± 13,97	114,93 ± 11,05	NS	0,001	0,001

Information	8,36 ± 3,06	7,42 ± 3,34	11,08 ± 2,67	NS	0,001	0,001
Similarities	9,05 ± 3,44	8,74 ± 3,56	13,15 ± 3,15	NS	0,001	0,001
Arithmetic	9,88 ± 3,11	8,62 ± 3,69	11,82 ± 2,55	NS	0,001	0,004
Vocabulary	11,19 ±3,94	10,20 ± 5,95	15,74 ± 2,48	NS	0,001	0,001
Comprehension	9,13 ± 3,24	8,97 ± 3,69	12,17 ± 2,39	NS	0,001	0,001
Puzzle	9,08 ± 2,72	8,48 ± 2,69	11,18 ± 2,32	NS	0,001	0,001
Picture stories	10,22 ± 3,90	10,11 ± 4,30	10,81 ± 2,18	NS	NS	NS
Block design	9,75 ± 4,24	9,88 ± 3,93	11,20 ± 2,36	NS	0,040	NS
Picture completion	11,08 ± 2,76	10,45 ± 3,11	12,12 ± 2,79	NS	0,009	NS
Coding	10,33 ± 3,74	9,34 ± 5,28	11,89 ± 2,33	NS	0,001	0,003

Total intelligence quotient, T-IQ ; Performance intelligence quotient, P-IQ ; Verbal intelligence quotient, V-IQ.

Table 3. Correlation between intelligence quotients and age of onset of disease, duration of disease, BMI percentile and respiratory disturbance index in obese children.

	Age of onset of disease (years)	Duration of disease (months)	BMI Percentile	RDI (ev/h)
V-QI	r = 0,335*	r = -0,362*	NS	NS
P-QI	NS	NS	r = -0,341*	NS
T-QI	NS	NS	NS	r = -0,321*

Total intelligence quotient, T-IQ ; Performance intelligence quotient, P-IQ ; Verbal intelligence quotient, V-IQ; Respiratory disturbance index, RDI ; Body mass index BMI

*p<0,05

Table 4. Children with hyperactivity and inattention symptoms in the different groups

	Children with obstructive sleep apnea syndrome (group1+group 2) N=74	Non obese children with obstructive sleep apnea syndrome (Group 1) N=36	Children with obstructive sleep apnea syndrome and obesity (Group 2) N=38	Control group (Group 3) N=58	χ2 test (1 vs 2)
Hyperactivity	20/74 (27%)	13/36 (36,1%)	7/38 (18,5%)	0/58	NS
Inattention	21/74 (28,3%)	12/36 (33%)	9/38 (23,7%)	0/58	NS

Table 5- Stepwise multiple linear regression analysis in children with obstructive sleep apnea syndrome and obesity (Group 2). Significative values for p<0.05

Dependent variable	**Significant variable**	**Standardized β coefficients**	**p**
T-IQ	RDI (ev/h)	-0,35	0,048
	Duration of disease (years)	-0,50	NS
	Symptoms onset (years)	-0,48	NS
	BMI(kg/m^2)	0,58	NS

	BMI percentile	-0,72	0,05

Total intelligence quotient, T-IQ ; Respiratory disturbance index, RDI ; Body mass index BMI